

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents  
United States Patent and Trademark  
Office  
Box PCT  
Washington, D.C. 20231  
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

|                                                                                  |                                                                      |
|----------------------------------------------------------------------------------|----------------------------------------------------------------------|
| <b>Date of mailing</b> (day-month-year)<br>03 October 2000 (03.10.00)            |                                                                      |
| <b>International application No.</b><br>PCT/GB00/00281                           | <b>Applicant's or agent's file reference</b><br>PCB/D088334PWO       |
| <b>International filing date</b> (day-month-year)<br>01 February 2000 (01.02.00) | <b>Priority date</b> (day-month-year)<br>05 February 1999 (05.02.99) |
| <b>Applicant</b><br>POMFRETT, Christopher, John, Douglas et al                   |                                                                      |

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:  
01 September 2000 (01.09.00)

☐ in a notice effecting later election filed with the International Bureau on:  
\_\_\_\_\_

2. The election ☒ was  
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

|                                                                                               |                                |
|-----------------------------------------------------------------------------------------------|--------------------------------|
| The International Bureau of WIPO<br>34, chemin des Colombettes<br>1211 Geneva 20, Switzerland | Authorized officer<br>S. Mafia |
| Facsimile No. (41-22) 740 14 35                                                               | Telex No. (41-22) 53503 GOS    |

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
10 August 2000 (10.08.2000)

PCT

(10) International Publication Number  
**WO 00/45832 A3**

(51) International Patent Classification<sup>7</sup>: **A61K 38/08**,  
A61P 23/00

(74) Agent: **BANFORD, Paul, Clifford**; Marks & Clerk,  
Sussex House, 83-85 Mosley Street, Manchester M2 3LG  
(GB).

(21) International Application Number: PCT/GB00/00281

(22) International Filing Date: 1 February 2000 (01.02.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
9902469.7 5 February 1999 (05.02.1999) GB  
60/120,326 17 February 1999 (17.02.1999) US  
60/155,661 24 September 1999 (24.09.1999) US

(81) Designated States (*national*): AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

(71) Applicant (*for all designated States except US*): **THE VICTORIA UNIVERSITY OF MANCHESTER** [GB/GB]; Oxford Road, Manchester M13 9PL (GB).

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **POMFRETT, Christopher, John, Douglas** [GB/GB]; 17 Manifold Close, Elworth, Sandbach, Cheshire CW11 1XP (GB). **ALKIRE, Michael** [US/US]; 2959 Java Road, Costa Mesa, CA 92626 (US). **HAIER, Richard** [US/US]; 10 Harvey Court, Irvine, CA 92612 (US). **FALLON, Jim** [US/US]; 5 Dickens Court, Irvine, CA 92612 (US).

**Published:**

- With international search report.
- Before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments.

(88) Date of publication of the international search report:  
30 November 2000

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(54) Title: REGULATION OF ANAESTHESIA

(57) Abstract: The present invention concerns uses of compounds which modulate Delta-Sleep Inducing Peptide active for regulating anaesthesia and methods of evaluating the anaesthetic needs of a subject comprising assaying a sample taken from the subject for the presence of Delta-Sleep Inducing Peptide.



**WO 00/45832 A3**

**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

|    |                          |    |                                          |    |                                              |    |                          |
|----|--------------------------|----|------------------------------------------|----|----------------------------------------------|----|--------------------------|
| AL | Albania                  | ES | Spain                                    | LS | Lesotho                                      | SI | Slovenia                 |
| AM | Armenia                  | FI | Finland                                  | LT | Lithuania                                    | SK | Slovakia                 |
| AT | Austria                  | FR | France                                   | LU | Luxembourg                                   | SN | Senegal                  |
| AU | Australia                | GA | Gabon                                    | LV | Latvia                                       | SZ | Swaziland                |
| AZ | Azerbaijan               | GB | United Kingdom                           | MC | Monaco                                       | TD | Chad                     |
| BA | Bosnia and Herzegovina   | GE | Georgia                                  | MD | Republic of Moldova                          | TG | Togo                     |
| BB | Barbados                 | GH | Ghana                                    | MG | Madagascar                                   | TJ | Tajikistan               |
| BE | Belgium                  | GN | Guinea                                   | MK | The former Yugoslav<br>Republic of Macedonia | TM | Turkmenistan             |
| BF | Burkina Faso             | GR | Greece                                   |    |                                              | TR | Turkey                   |
| BG | Bulgaria                 | HU | Hungary                                  | ML | Mali                                         | TT | Trinidad and Tobago      |
| BJ | Benin                    | IE | Ireland                                  | MN | Mongolia                                     | UA | Ukraine                  |
| BR | Brazil                   | IL | Israel                                   | MR | Mauritania                                   | UG | Uganda                   |
| BY | Belarus                  | IS | Iceland                                  | MW | Malawi                                       | US | United States of America |
| CA | Canada                   | IT | Italy                                    | MX | Mexico                                       | UZ | Uzbekistan               |
| CF | Central African Republic | JP | Japan                                    | NE | Niger                                        | VN | Viet Nam                 |
| CG | Congo                    | KE | Kenya                                    | NL | Netherlands                                  | YU | Yugoslavia               |
| CH | Switzerland              | KG | Kyrgyzstan                               | NO | Norway                                       | ZW | Zimbabwe                 |
| CI | Côte d'Ivoire            | KP | Democratic People's<br>Republic of Korea | NZ | New Zealand                                  |    |                          |
| CM | Cameroon                 | KR | Republic of Korea                        | PL | Poland                                       |    |                          |
| CN | China                    | KZ | Kazakhstan                               | PT | Portugal                                     |    |                          |
| CU | Cuba                     | LC | Saint Lucia                              | RO | Romania                                      |    |                          |
| CZ | Czech Republic           | LI | Liechtenstein                            | RU | Russian Federation                           |    |                          |
| DE | Germany                  | LK | Sri Lanka                                | SD | Sudan                                        |    |                          |
| DK | Denmark                  | LR | Liberia                                  | SE | Sweden                                       |    |                          |
| EE | Estonia                  |    |                                          | SG | Singapore                                    |    |                          |

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

|                                                                     |                                                                                                                                                         |                                                                |
|---------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------|
| Applicant's or agent's file reference<br><b>PCB/D088334PW0</b>      | <b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below. |                                                                |
| International application No.<br><b>PCT/GB 00/ 00281</b>            | International filing date (day/month/year)<br><b>01/02/2000</b>                                                                                         | (Earliest) Priority Date (day/month/year)<br><b>05/02/1999</b> |
| Applicant<br><br><b>THE VICTORIA UNIVERSITY OF MANCHESTER et al</b> |                                                                                                                                                         |                                                                |

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

**1. Basis of the report**

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☒ furnished subsequently to this Authority in written form.

☒ furnished subsequently to this Authority in computer readable form.

☒ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☒ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.

## FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-4, 8-9

Present claims 1-4 and 8-9 relate to a compound defined by reference to a desirable characteristic or property, namely the fact that it modulates (claims 1, 9), promotes/mimics (claims 2, 4) or inhibits (claim 8) Delta-Sleep inducing peptide activity.

The claims cover all compounds having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compounds. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compound by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the uses and methods claimed when the compound is Delta-Sleep inducing peptide self, including its phosphorylated and cyclic derivatives (see page 4 of the description) as well as Melatonin, Dalargin and Neokytorphin (see page 8 of the description).

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/00281

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K38/08 A61P23/00

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

BIOSIS, WPI Data, EPO-Internal, STRAND, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category * | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                                                                                                                                                                                                                                                           | Relevant to claim No. |
|------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| X          | <p>DATABASE BIOSIS 'Online!<br/> BIOSCIENCES INFORMATION SERVICE,<br/> PHILADELPHIA, PA, US; 1991<br/> SUDAKOV K V: "ANTISTRESS EFFECTS OF<br/> DELTA-SLEEP INDUCING PEPTIDE"<br/> Database accession no. PREV199294101504<br/> XP002146452<br/> abstract<br/> &amp; FIZIOLOGICHESKII ZHURNAL SSSR IMENI I M<br/> SECHENOVA,<br/> vol. 77, no. 3, 1991, pages 1-13,<br/> ISSN: 0015-329X</p> <p style="text-align: center;">---<br/>-/--</p> | 4-7                   |

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

\* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&amp;" document member of the same patent family

Date of the actual completion of the international search

4 September 2000

Date of mailing of the international search report

18/09/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo.nl,  
Fax: (+31-70) 340-3016

Authorized officer

Fernandez y Branas, F

## INTERNATIONAL SEARCH REPORT

International Application No.

PCT/GB 00/00281

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category | Citation of document, with indication, where appropriate, of the relevant passages                                                                                                                                                   | Relevant to claim No. |
|----------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------|
| X        | DATABASE WPI<br>Section Ch, Week 199840<br>Derwent Publications Ltd., London, GB;<br>Class B04, AN 1998-465470<br>XP002146453<br>& RU 2 104 717 C (NOVOK DOCTORS TRAINING<br>INST), 20 February 1998 (1998-02-20)<br>abstract<br>--- | 1-3,8,9               |
| X        | EP 0 513 702 A (BIELLA GABRIELE ;FRASCHINI<br>FRANCO (IT); STANVOK BOJIDAR (IT); FERI)<br>19 November 1992 (1992-11-19)<br>the whole document<br>---                                                                                 | 1-3,8,9               |
| A        | US 4 444 758 A (SCHERSCHLICHT RICHARD R<br>ET AL) 24 April 1984 (1984-04-24)<br>the whole document<br>---                                                                                                                            | 1-13                  |
| A        | US 4 165 312 A (SCHOENENBERGER GUIDO A)<br>21 August 1979 (1979-08-21)<br>the whole document<br>-----                                                                                                                                | 1-13                  |

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 00/00281

| Patent document<br>cited in search report |   | Publication<br>date | Patent family<br>member(s) | Publication<br>date |
|-------------------------------------------|---|---------------------|----------------------------|---------------------|
| RU 2104717                                | C | 20-02-1998          | NONE                       |                     |
| EP 0513702                                | A | 19-11-1992          | IT 1251544 B               | 17-05-1995          |
|                                           |   |                     | AT 142877 T                | 15-10-1996          |
|                                           |   |                     | AT 184792 T                | 15-10-1999          |
|                                           |   |                     | DE 69213814 D              | 24-10-1996          |
|                                           |   |                     | DE 69213814 T              | 03-04-1997          |
|                                           |   |                     | DE 69230046 D              | 28-10-1999          |
|                                           |   |                     | DE 69230046 T              | 31-05-2000          |
|                                           |   |                     | DK 513702 T                | 30-12-1996          |
|                                           |   |                     | EP 0713701 A               | 29-05-1996          |
|                                           |   |                     | ES 2093735 T               | 01-01-1997          |
|                                           |   |                     | ES 2139132 T               | 01-02-2000          |
|                                           |   |                     | GR 3022060 T               | 31-03-1997          |
|                                           |   |                     | JP 5155769 A               | 22-06-1993          |
|                                           |   |                     | US 5430029 A               | 04-07-1995          |
| US 4444758                                | A | 24-04-1984          | AU 552547 B                | 05-06-1986          |
|                                           |   |                     | AU 8375682 A               | 25-11-1982          |
|                                           |   |                     | CA 1188989 A               | 18-06-1985          |
|                                           |   |                     | DE 3218761 A               | 16-12-1982          |
|                                           |   |                     | EP 0065747 A               | 01-12-1982          |
|                                           |   |                     | IE 53395 B                 | 09-11-1988          |
|                                           |   |                     | IL 65782 A                 | 30-08-1985          |
|                                           |   |                     | IT 1152116 B               | 31-12-1986          |
|                                           |   |                     | JP 1688906 C               | 11-08-1992          |
|                                           |   |                     | JP 3054089 B               | 19-08-1991          |
|                                           |   |                     | JP 58023630 A              | 12-02-1983          |
|                                           |   |                     | PH 17981 A                 | 26-02-1985          |
|                                           |   |                     | US 4496545 A               | 29-01-1985          |
|                                           |   |                     | ZA 8203369 A               | 30-03-1983          |
| US 4165312                                | A | 21-08-1979          | CH 634331 A                | 31-01-1983          |
|                                           |   |                     | DE 2828433 A               | 11-01-1979          |
|                                           |   |                     | FR 2396016 A               | 26-01-1979          |
|                                           |   |                     | GB 2000511 A, B            | 10-01-1979          |
|                                           |   |                     | JP 1468817 C               | 30-11-1988          |
|                                           |   |                     | JP 54039050 A              | 24-03-1979          |
|                                           |   |                     | JP 63017840 B              | 15-04-1988          |



REFLAGE  
ART 34 ANNEXCLAIMS

1. The use of a compound which modulates Delta-Sleep Inducing Peptide activity for the manufacture of a medicament for regulating anaesthesia.
2. The use according to claim 1, wherein the compound promotes or mimics Delta-Sleep Inducing Peptide activity and the medicament promotes or induces anaesthesia.
3. The use according to claim 2 wherein the compound is for use in conjunction with another anaesthetic agent.
4. The use of a compound which promotes Delta-Sleep Inducing Peptide activity for the manufacture of a medicament for promoting or inducing sedation.
5. The use according to any one of claims 2 - 4, wherein the compound is Delta-Sleep Inducing Peptide or biologically active fragments and derivatives thereof.
6. The use according to claim 5 wherein the compound is a nonapeptide with the amino acid sequence:  
Trp-Ala-Gly-Gly-Asp-Ala-Ser-Gly-Glu  
- or biologically active fragments and derivatives thereof.
7. The use according to claim 6 wherein at least one amino acid or derivative thereof is phosphorylated.
8. The use according to claim 1, wherein the compound inhibits Delta-Sleep Inducing Peptide activity and the medicament promotes or induces recovery from anaesthesia.

9. A method of regulating anaesthesia comprising administering to a subject in need of treatment a compound which modulates Delta-Sleep Inducing Peptide activity.
10. A method of evaluating the anaesthetic needs of a subject to be anaesthetised comprising assaying a sample taken from the subject for the presence of Delta-Sleep Inducing Peptide.
11. The method according to claim 10, wherein the sample is a blood or urine sample.
12. The method according to claim 10 or 11, wherein higher than average endogenous levels of Delta-Sleep Inducing Peptide assayed from the sample indicate the subject will have lower than average anaesthetic requirements.
13. The method according to claim 10 or 11, wherein lower than average endogenous levels of Delta-Sleep Inducing Peptide assayed from the sample indicate the subject will have higher than average anaesthetic requirements.

09/892721

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

|                                                                                           |                                                                                                                               |                                              |
|-------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------|
| Applicant's or agent's file reference<br>PCB/D088334PWO                                   | <b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416) |                                              |
| International application No.<br>PCT/GB00/00281                                           | International filing date (day/month/year)<br>01/02/2000                                                                      | Priority date (day/month/year)<br>05/02/1999 |
| International Patent Classification (IPC) or national classification and IPC<br>A61K38/08 |                                                                                                                               |                                              |
| Applicant<br>THE VICTORIA UNIVERSITY OF MANCHESTER et al                                  |                                                                                                                               |                                              |

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 6 sheets, including this cover sheet.

- ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

|                                                                                                                                                                                                                                                                                     |                                                                                                                                                          |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------|
| Date of submission of the demand<br>01/09/2000                                                                                                                                                                                                                                      | Date of completion of this report<br>18.01.2001                                                                                                          |
| Name and mailing address of the international preliminary examining authority:<br> European Patent Office<br>D-80298 Munich<br>Tel. +49 89 2399 - 0 Tx: 523656 epmu d<br>Fax: +49 89 2399 - 4465 | Authorized officer<br>Deck, A<br><br>Telephone No. +49 89 2399 8422 |

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

BANFORD, Paul C.  
MARKS & CLERK  
Sussex House  
83-85 Mosley Street  
Manchester M2 3LG  
GRANDE BRETAGNE

## PCT

NOTIFICATION OF TRANSMITTAL OF  
THE INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT  
(PCT Rule 71.1)

Date of mailing  
(day/month/year) 18.01.2001

Applicant's or agent's file reference  
PCB/D088334PWO ✓

### IMPORTANT NOTIFICATION

International application No.  
PCT/GB00/00281

International filing date (day/month/year)  
01/02/2000

Priority date (day/month/year)  
05/02/1999

Applicant

THE VICTORIA UNIVERSITY OF MANCHESTER et al

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

#### 4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/



European Patent Office  
D-80298 Munich  
Tel +49 89 2399 - 0 Tx: 523556 epmu d  
Fax: +49 89 2399 - 4465

Authorized officer

Hundt, D

Tel. +49 89 2399-8042



INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT

International application No. PCT/GB00/00281

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).)*:  
Description, pages:

1-15 as originally filed

Claims, No.:

1-12 as received on 14/12/2000 with letter of 14/12/2000

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/00281

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

### III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.

- ☒ claims Nos. 9-12.

because:

- ☒ the said international application, or the said claims Nos. 9-12 relate to the following subject matter which does not require an international preliminary examination (*specify*):  
see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

- ☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination report cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions;

- ☐ the written form has not been furnished or does not comply with the standard.

- ☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

### 1. Statement

Novelty (N)                      Yes:    Claims    1-12  
                                             No:    Claims

|                     |      |        |      |
|---------------------|------|--------|------|
| Inventive step (IS) | Yes: | Claims | 1-12 |
|                     | No:  | Claims |      |

Industrial applicability (IA) Yes: Claims 1-8

INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT

International application No. PCT/GB00/00281

No: Claims

2. Citations and explanations  
see separate sheet

INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET

International application No. PCT/GB00/00281

Concerning section III:

Claims 9-12 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Concerning section V:

The following documents are referred to in this communication; the numbering will be adhered to in the rest of the procedure:

- D1: DATABASE BIOSIS [Online] BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US; 1991 SUDAKOV K V: 'ANTISTRESS EFFECTS OF DELTA-SLEEP INDUCING PEPTIDE' Database accession no. PREV199294101504 XP002146452 & FIZIOLOGICHESKII ZHURNAL SSSR IMENI I M SECHENOVA, vol. 77, no. 3, 1991, pages 1-13, ISSN: 0015-329X
- D2: DATABASE WPI Section Ch, Week 199840 Derwent Publications Ltd., London, GB; Class B04, AN 1998-465470 XP002146453 & RU 2 104 717 C (NOVOK DOCTORS TRAINING INST), 20 February 1998 (1998-02-20)
- D3: EP-A-0 513 702 (BIELLA GABRIELE ;FRASCHINI FRANCO (IT); STANVOK BOJIDAR (IT); FERI) 19 November 1992 (1992-11-19)

D1 describes the antistress activity of DSIP.

D2 discloses the use of dalargin, a DSIP antagonist according to the present invention, for protecting patients with Leriche's syndrome during operations.

D3 describes the use of melatonin, another DSIP antagonist according to the present invention, in the therapy of sleep disorders and in the pre-anaesthetic medication.

None of the prior art documents describe the use of DSIP or biologically active fragments and derivatives thereof for the manufacture of a medicament for regulating anaesthesia, not for evaluating the anaesthetic needs of a subject.

The subject-matter of claims 1 to 12 is therefore new.



INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET

International application No. PCT/GB00/00281

The closest prior art is the document D3 which describes the use of a compound which modulates DSIP activity for inducing sedation or in the pre-anaesthetic medication.

The problem underlying the invention is to find new compounds useful either for inducing anaesthesia or for promoting recovery from anaesthesia.

The invention solves the problem, the solution being the use of the nonapeptide DSIP itself (or derivatives) for inducing anaesthesia or sedation, and the use of DSIP antagonists to promote recovery from anaesthesia.

The subject-matter of claims 1 to 12 is inventive because

- the anaesthetic activity of DSIP is neither taught nor suggested in the available prior art;
- DSIP antagonists, e.g. melatonin or dalargin, are only described for anaesthetizing patients, not for promoting their recovery from anaesthesia;
- a method of evaluating the anaesthetic needs of a subject by assessing the presence of DSIP in a sample is neither described nor suggested in the prior art.

Industrial applicability:

For the assessment of the present claims 9-12 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

CLAIMS

1. The use of Delta-Sleep Inducing Peptide or biologically active fragments and derivatives thereof for the manufacture of a medicament for regulating anaesthesia.
2. The use according to claim 1 for promoting or inducing anaesthesia.
3. The use according to claim 1 for promoting or inducing sedation.
4. The use according to any preceding claim wherein the compound is for use in conjunction with another anaesthetic agent.
5. The use according to any preceding claim wherein the compound is a nonapeptide with the amino acid sequence:  
Trp-Ala-Gly-Gly-Asp-Ala-Ser-Gly-Glu  
- or biologically active fragments and derivatives thereof.
6. The use according to claim 5 wherein at least one amino acid or derivative thereof is phosphorylated.
7. The use of a compound that decreases Delta-Sleep Inducing Peptide activity for the manufacture of a medicament for promoting or inducing recovery from anaesthesia.
8. The use according to claim 7 wherein the compound is melatonin, dalargin or neokytorphin..
9. A method of evaluating the anaesthetic needs of a subject to be anaesthetised comprising assaying a sample taken from the subject for the presence of Delta-Sleep Inducing Peptide.

10. The method according to claim 9, wherein the sample is a blood or urine sample.

11. The method according to claim 9 or 10, wherein higher than average endogenous levels of Delta-Sleep Inducing Peptide assayed from the sample indicate the subject will have lower than average anaesthetic requirements.

12. The method according to claim 9 or 10, wherein lower than average endogenous levels of Delta-Sleep Inducing Peptide assayed from the sample indicate the subject will have higher than average anaesthetic requirements.